Supporting information

Amorphous calcium pyrophosphate bone cement sets without crystallization: A physico-chemical and *in vitro* biological study

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Supplementary Figures, Tables :
9 Pages : 9 Figures, 2 Tables

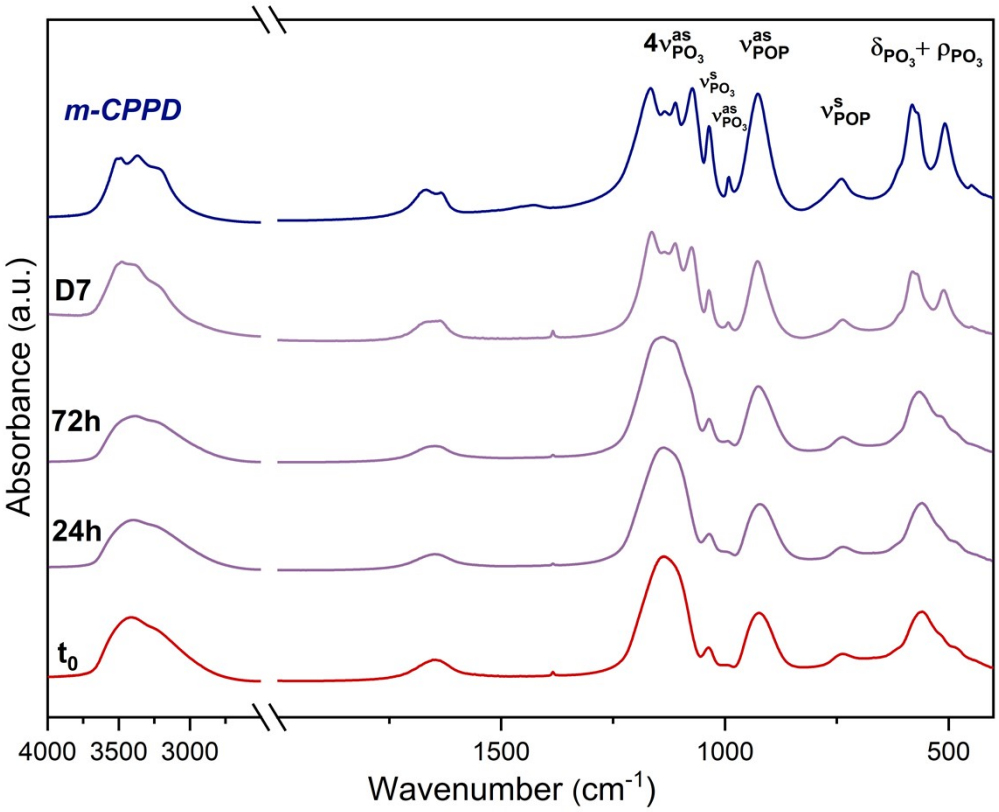

Figure S1: FTIR spectra in 400-4000 cm^{-1} region of the a-CPPc cement paste during its setting and hardening, between t_0 to 7 days, with identification of the vibrational bands of pyrophosphate groups.

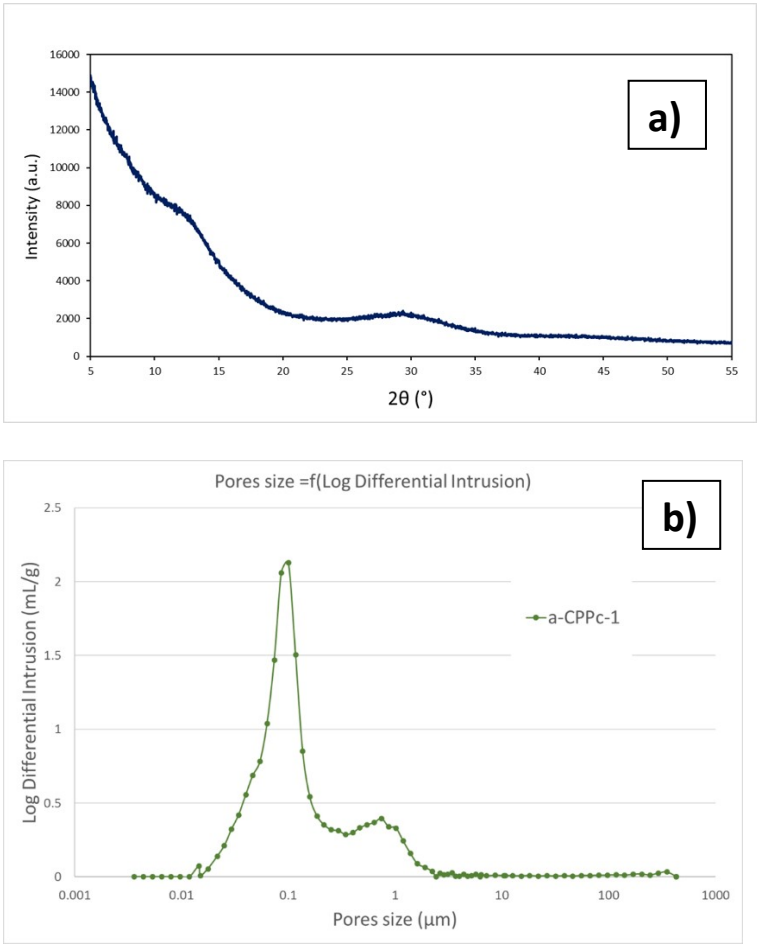

Figure S2: a) X-ray diffractogram, and b) Pore size distribution of the fully amorphous a-CPPDc cement (obtained after 24 hours of cement paste maturation at 37°C in wet atmosphere and then drying).

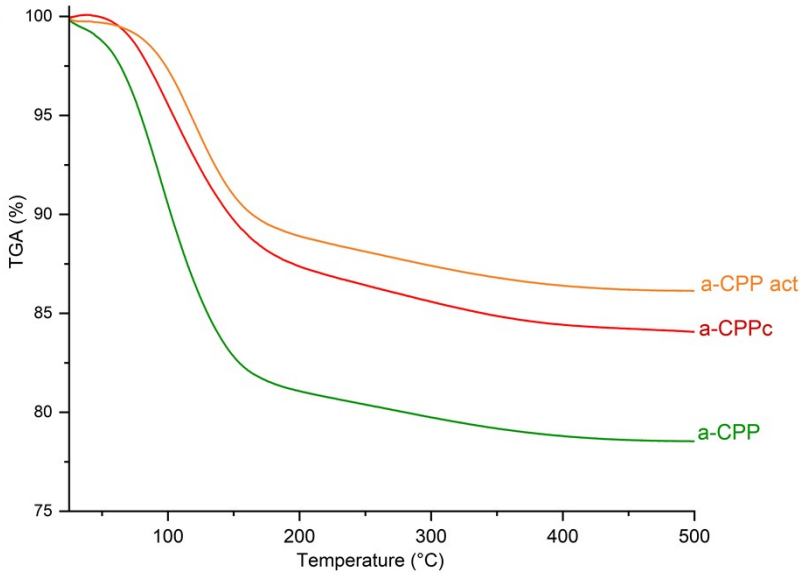

Figure S3: TGA curve from 25°C to 500°C of amorphous CPP before (a-CPP) and after thermal treatment 1h at 100°C (a-CPP act) and of the a-CPPc cement (a-CPPc dried after 48 h of maturation time at 37°C in wet atmosphere).

Table S1: ^{1}H and ^{31}P isotropic chemical shifts of the various amorphous calcium pyrophosphate samples: a-CPP and associated a-CPP act and a-CPPc.

SAMPLES	a-CPP	a-CPP act	a-CPPc
δ_{iso} ^{1}H (ppm)	5.50 0.26	4.99 0.23	5.42 3.83 1.24 0.17
δ_{iso} ^{31}P (ppm)	-6.79	-6.96	-6.60
Shoulder [0-8] ppm	Very low	More intense	More intense

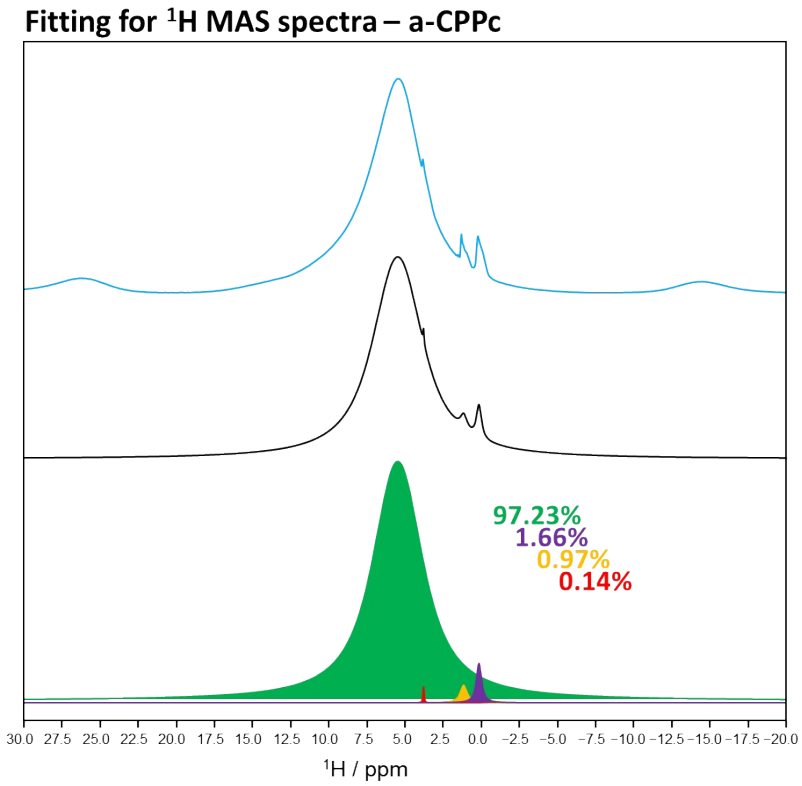

Figure S4: Experimental (blue) and simulated (black) ^{1}H MAS NMR spectrum and the simulation decomposition (bottom) obtained for the a-CPPc sample. The peaks at 1.24 and 3.83 ppm are associated with the ethanol residues used to wash the rotor.

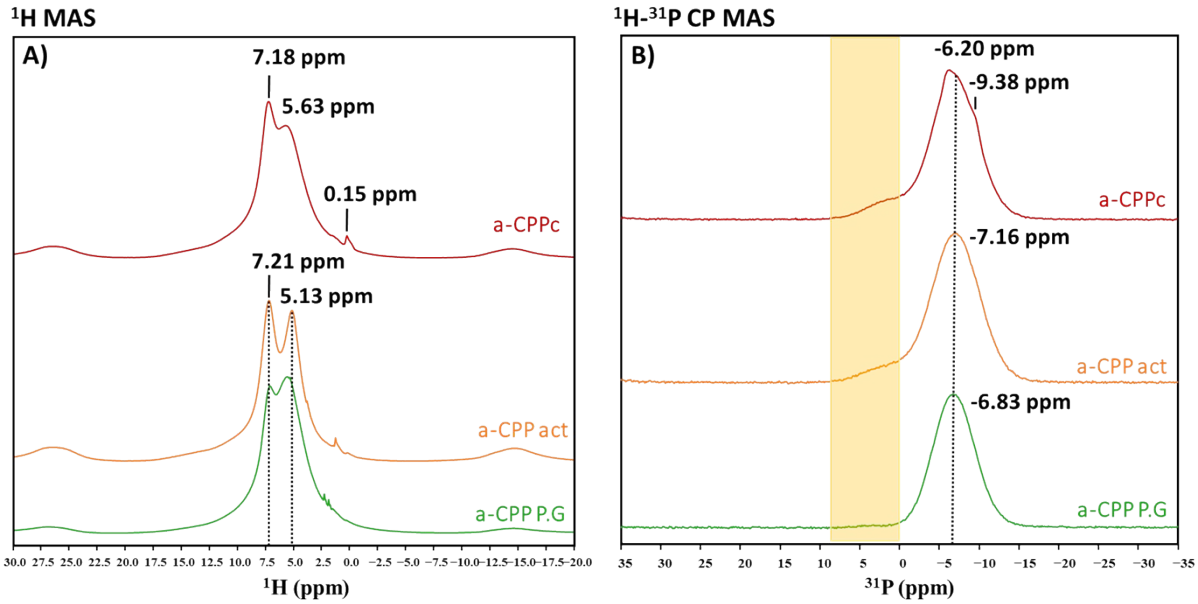

Figure S5: ^{1}H MAS and ^{1}H-^{31}P CP MAS NMR spectra of the various amorphous calcium pyrophosphate samples involved in a-CPPc preparation: a-CPP P.G (synthesized according to the P.G. protocol)[1] and its related a-CPP act and a-CPPc samples. On right spectra, the yellow band show [0-8 ppm] range.

Table S2: ^{1}H and ^{31}P isotropic chemical shifts of the various amorphous calcium pyrophosphate samples involved in a-CPPc preparation: a-CPP P.G (synthesized according to the P.G. protocol)[1] and its related a-CPP act and a-CPPc.

SAMPLES	a-CPP P.G	a-CPP act	a-CPPc
δ_{iso} ^{1}H (ppm)	7.10 5.58 2.25 1.80	7.21 5.13 3.79 1.29 0.20	7.18 5.63 0.15 (+ shoulder)
δ_{iso} ^{31}P (ppm)	-6.83	-7.16	-6.20 ≈ -9.38
Shoulder [0-8] ppm	Very low	More intense	More intense

Raman spectra of a-CPPc cement before and after 7 and 15 days of immersion in SBF solution (Figure S5) shows a band at 955 cm^{-1} related to $\nu^{s}PO_4$ of orthophosphate ions which are present in apatite samples. This band is more intense after 15 days in SBF and can correspond to a higher proportion of orthophosphate ions in a-CPPc cement disk.

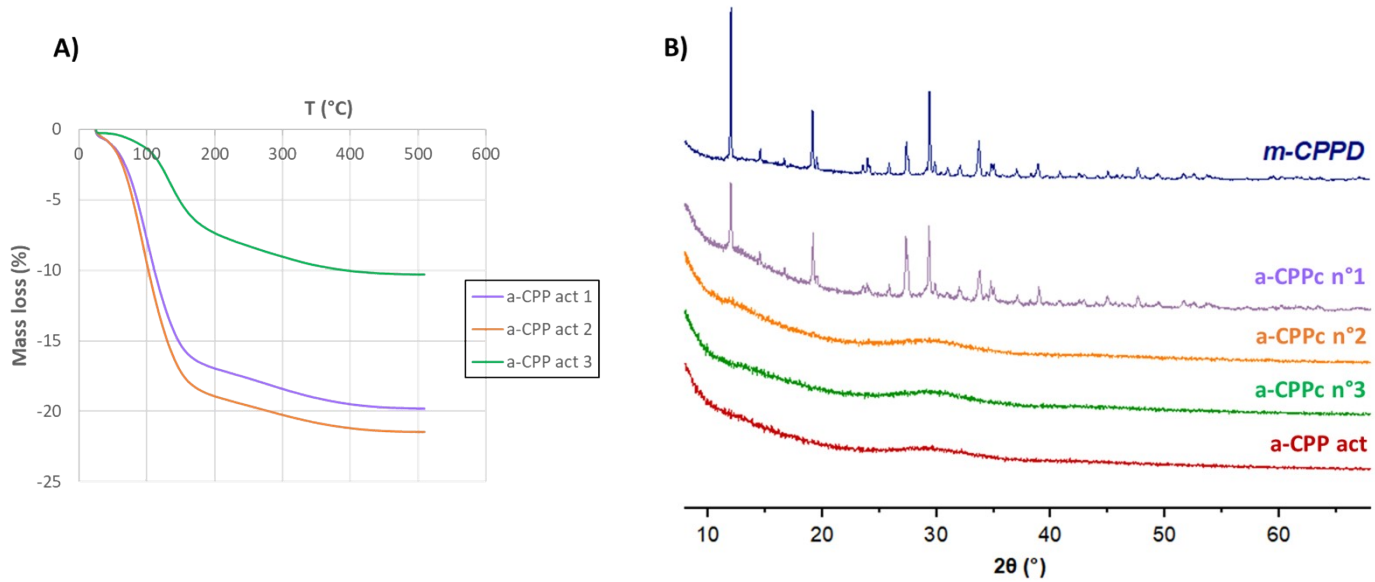

Figure S6: A) TGA curves of a-CPP act samples (n°1, 2 and 3) dried by using three different processes or duration as reported in Table 5. B) X-ray diffractograms of the corresponding a-CPPc cements after one week of maturation at 37°C in wet atmosphere compare to those of a-CPP act and of m-CPPD reference sample. a-CPPc cements n°1, 2 and 3 were prepared from a-CPP act obtained from a-CPP dried using three different processes or duration as reported in Table 5.

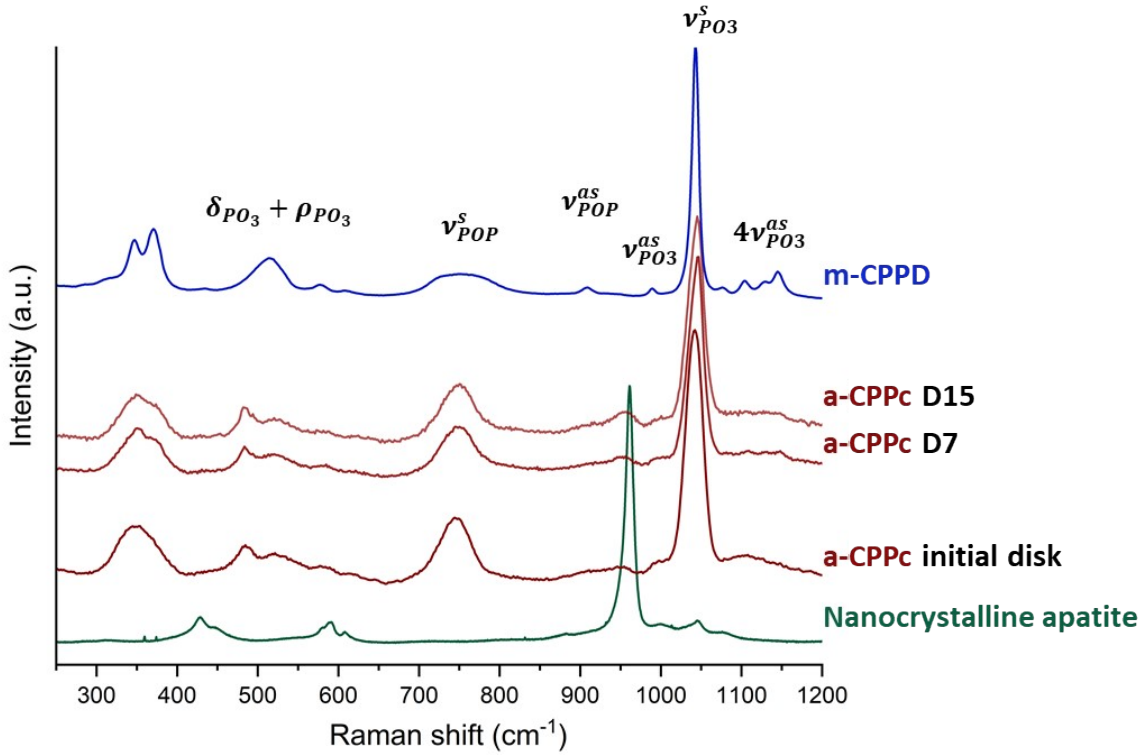

Figure S7: Raman spectra of a-CPPc cement before and after immersion in SBF medium for 7 and 15 days. The spectrum of pure m-CPPD phase and nanocrystalline apatite are also shown.

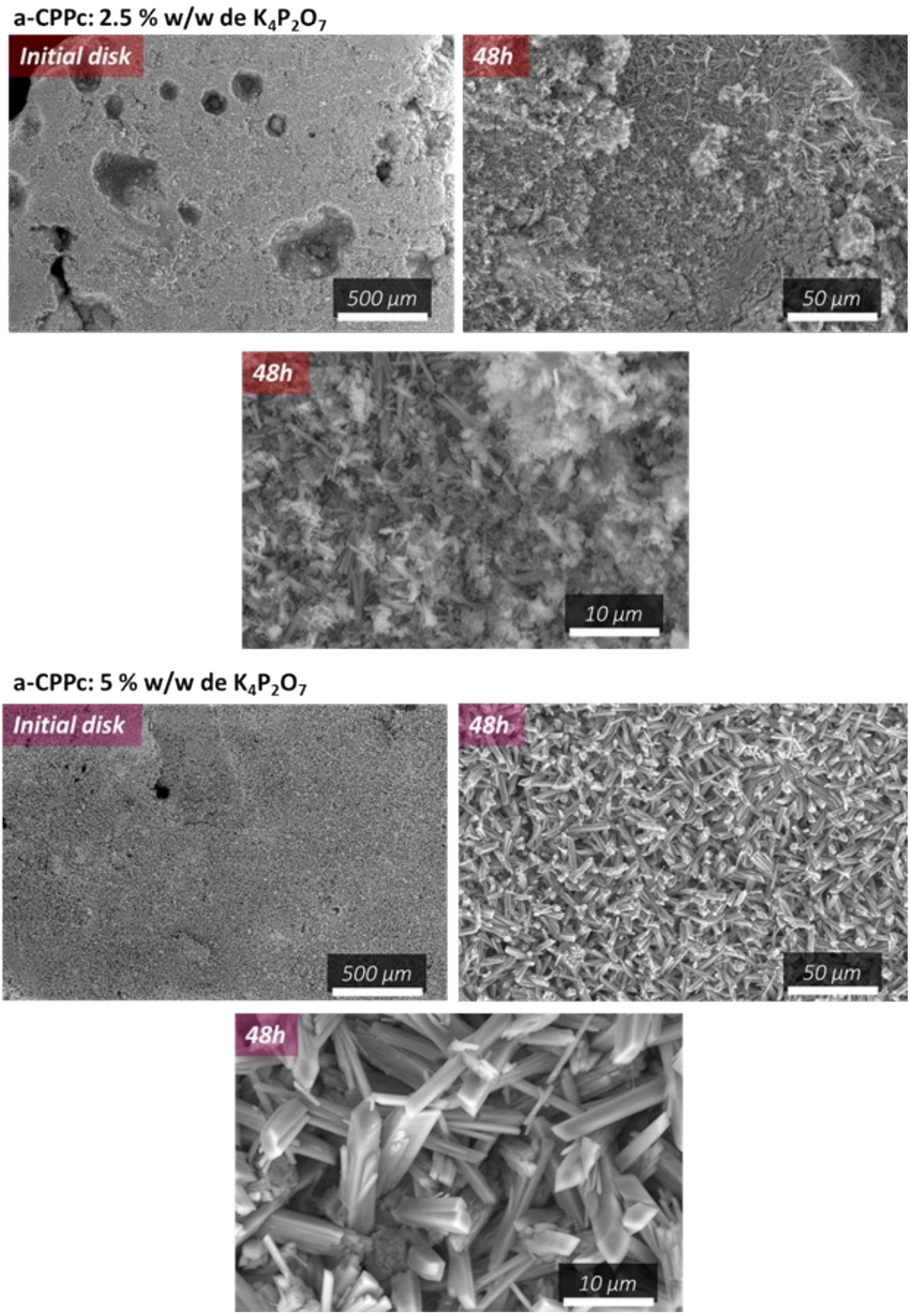

Figure S8: SEM micrographs of a-CPPc cements prepared with a liquid phase containing 2.5 % w/w $K_4P_2O_7$ (top) or 5 % w/w $K_4P_2O_7$ (bottom), before and after 48 hours of immersion in EMEM serum-free cell culture medium.

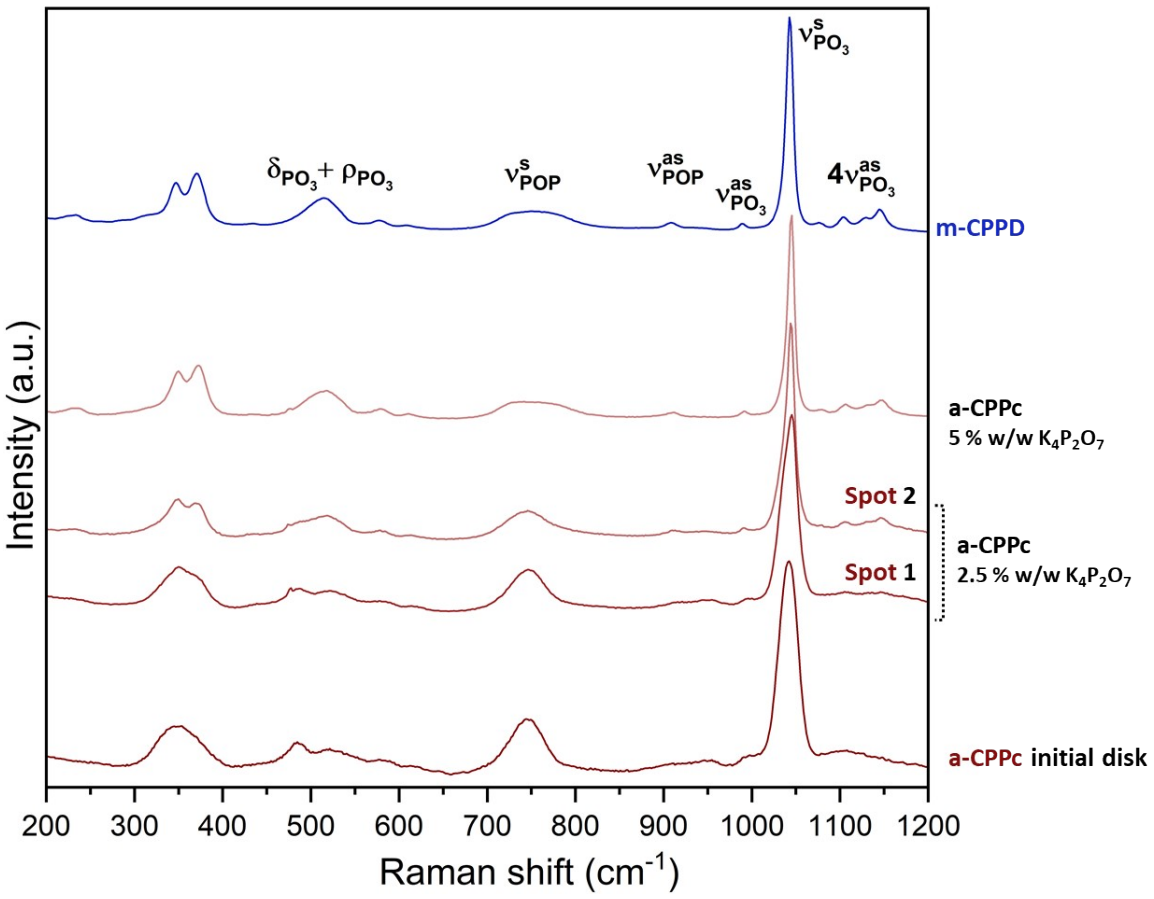

Figure S9: Raman spectra a-CPPc cement prepared with a liquid phase containing 2.5 % w/w $K_4P_2O_7$ or 5 % w/w $K_4P_2O_7$ before and after 48 hours of immersion in EMEM serum-free cell culture medium. The spectrum of pure m-CPPD phase is also shown.

Reference

(1) Gras, P.; Rey, C.; Marsan, O.; Sarda, S.; Combes, C. Synthesis and Characterisation of Hydrated Calcium Pyrophosphate Phases of Biological Interest. *Eur. J. Inorg. Chem.* **2013**, *2013* (34), 5886–5895. https://doi.org/10.1002/ejic.201300955.